

***What is claimed is:***

1. A method of identifying one or more markers for schizophrenia, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

5 a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having said schizophrenia, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for schizophrenia; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals not having schizophrenia,

10 wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for schizophrenia.

2. A method of identifying one or more markers for schizophrenia, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

15 a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having schizophrenia, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for schizophrenia; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals having schizophrenia,

20 wherein those compared transcripts which display the same levels in the comparison of step b) are identified as being markers for schizophrenia.

3. A method of identifying one or more markers of a stage of Schizophrenia progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

25 a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of schizophrenia., wherein said one or more individuals are at the same progressive or regressive stage of schizophrenia., and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of Schizophrenia, and;

30 b) comparing the level of each of said one or more gene transcripts from said step a)

with the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of schizophrenia distinct from that of said one or more individuals of step a),

wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for the stage of progression or regression of Schizophrenia.

4. A method of identifying one or more markers of a stage of schizophrenia progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of schizophrenia, wherein said one or more individuals are at the same progressive or regressive stage of schizophrenia, and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of schizophrenia, and;

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of schizophrenia identical to that of said one or more individuals of step a),

wherein those compared transcripts which display the same levels in the comparison of step b) are identified as being markers for the stage of progression or regression of Schizophrenia.

5. A method of identifying one or more markers for distinguishing schizophrenia from manic depression syndrome, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having schizophrenia, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for schizophrenia; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals having manic depression syndrome, but not having schizophrenia,

wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for distinguishing schizophrenia from manic depression syndrome.

6. A method of identifying one or more markers for distinguishing schizophrenia from manic depression syndrome, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having schizophrenia, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for schizophrenia; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals having manic depression syndrome and not schizophrenia

c) comparing the level of each of said one or more gene transcripts from step a) with the level of each of said one or more gene transcripts in blood obtained from one or more individuals having neither manic depression syndrome nor schizophrenia,

wherein those compared transcripts which display differing levels in the comparison of step b) and step c) are identified as being markers for distinguishing schizophrenia from manic depression syndrome.

7. The method of any one of claims 1 - 6, wherein each of said one or more markers identifies one or more transcripts of one or more non immune response genes.

8. The method of any one of claims 1 - 6, wherein each of said one or more markers identifies a transcript of a gene expressed by non-blood tissue.

9. The method of any one of claims 1 - 6, wherein each of said one or more markers identifies a transcript of a gene expressed by non-lymphoid tissue.

10. The method of any one of claims 1 - 6, wherein said one or more markers identifies a sequence selected from the sequences listed in Table 3Y and Table 3AC.

11. A method of diagnosing or prognosing schizophrenia in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals not having schizophrenia,

wherein detecting a difference in the levels of each of said one or more gene transcripts in the comparison of step b) is indicative of schizophrenia in the individual of step a).

12. A method of diagnosing or prognosing schizophrenia in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts in blood obtained from said individual, wherein said one or more transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having schizophrenia,

wherein detecting the same levels of each of said one or more gene transcripts in the comparison of step b) is indicative of schizophrenia in the individual of step a).

13. A method of determining a stage of disease progression or regression in an individual having schizophrenia, comprising the steps of:

a) determining the level of one or more gene transcripts in blood obtained from said individual having schizophrenia, wherein said one or more transcripts correspond to said one or more markers of claim 3 and claim 4, and

b) comparing the level of each if said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood obtained from one or more individuals who each have been diagnosed as being at the same progressive or regressive stage of schizophrenia,

wherein the comparison from step b) allows the determination of the stage of schizophrenia progression or regression in an individual.

14. A method of diagnosing an individual as having schizophrenia as compared with manic depression syndrome, comprising the steps of:

a) determining the level of one or more gene transcripts in blood obtained from said individual having schizophrenia, wherein said one or more gene transcripts corresponds to said one or more markers of claim 5 and claim 6, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood obtained from one or more individuals who have manic depression syndrome,

wherein the comparison from step b) allows the determination of whether said individual has schizophrenia or manic depression syndrome.

15. A method of diagnosing or prognosing schizophrenia in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more transcripts corresponds to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having schizophrenia,

c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals not having schizophrenia

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said transcripts in step c)

wherein said determination is indicative of said individual of step a) having schizophrenia.

16. A method of determining a stage of disease progression or regression in an individual having schizophrenia, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts corresponds to said one or

more markers of claim 3 and claim 4, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having said stage of schizophrenia,

5 c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals not having said stage of schizophrenia,

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said  
10 transcripts in step c)

wherein said determination is indicative of said individual of step a) having said stage of schizophrenia.

17. A method of diagnosing an individual as having schizophrenia or manic depression syndrome, comprising the steps of:

15 a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 5 and claim 6, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from  
20 one or more individuals having schizophrenia,

c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having manic depression syndrome,

d) determining whether the levels of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with the levels of said  
25 transcripts in step c)

wherein said determination is indicative of said individual of step a) having schizophrenia.

18. A method of diagnosing an individual as having schizophrenia or manic depression syndrome, comprising the steps of:

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a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 5 and claim 6, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having schizophrenia,

c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having manic depression syndrome,

d) determining whether the levels of said one or more gene transcripts of step a) classify with the levels of said transcripts in step c) as compared with the levels of said transcripts in step b)

wherein said determination is indicative of said individual of step a) having manic depression syndrome.

19. The method of any one of claims 11 - 18, wherein said one or more gene transcripts are transcribed from one or more genes selected from the group consisting of the genes listed in Table 3Y and Table 3AC.

20. The method of any one of claims 1 - 6 and 11 - 18, wherein said one or more gene transcripts are transcribed from one or more genes selected from the group consisting of:

- a) non-immune response genes,
- b) genes expressed by non blood tissue, and
- c) genes expressed by non lymphoid tissue.

21. The method of any one of claims 1 - 6 and 11 - 18, wherein said blood comprises a blood sample obtained from said one or more individuals.

22. The method of claim 21, wherein said blood sample consists of whole blood.

23. The method of claim 21, wherein said blood sample consists of a drop of blood.

24. The method of claim 21, wherein said blood sample consists of blood that has been lysed.

25. The method of claim 21, further comprising the step of isolating RNA from said blood samples.
26. The method of any one of claims 1 - 6 and 11 - 18, wherein the step of determining the level of each of said one or more gene transcripts comprises quantitative RT-PCR (QRT-PCR), wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 6 and 11 - 18.
27. The method of claim 26, wherein said QRT-PCR comprises primers which hybridize to said one or more transcripts or the complement thereof, wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 6 and 11 - 18.
28. The method of claim 27, wherein said primers are 15-25 nucleotides in length.
29. The method of claim 27, wherein said primers hybridize to one or more genes selected from the group consisting of the genes listed in Table 3Y and Table 3AC, or the complement thereof.
30. The method of any one of claims 1 - 6 and 11 - 18, wherein the step of determining the level of each of said one or more gene transcripts comprises hybridizing a first plurality of isolated nucleic acid molecules that correspond to said one or more transcripts, to an array comprising a second plurality of isolated nucleic acid molecules.
31. The method of claim 30, wherein said first plurality of isolated nucleic acid molecules comprises RNA, DNA, cDNA, PCR products or ESTs.
32. The method of claim 30, wherein said array comprises a plurality of isolated nucleic acid molecules comprising RNA, DNA, cDNA, PCR products or ESTs.
33. The method of claim 32, wherein said array comprises two or more of the markers of claim 1.
34. The method of claim 32, wherein said array comprises two or more of the markers of claim 2.



35. The method of claim 32, wherein said array comprises two or more of the markers of claim 3.
36. The method of claim 32, wherein said array comprises two or more of the markers of claim 4.
- 5 37. The method of claim 32 wherein said array comprises two or more of the markers of claim 5.
38. The method of claim 32 wherein said array comprises two or more of the markers of claim 6.
39. The method of claim 32, wherein said array comprises a plurality of nucleic acid  
10 molecules that correspond to genes of the human genome.
40. The method of claim 32, wherein said array comprises a plurality of nucleic acid molecules that correspond to two or more genes selected from the group consisting of the genes listed in Table 3Y and Table 3AC.
41. A plurality of isolated nucleic acid molecules that correspond to two or more of the  
15 markers of claim 1.
42. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 2.
43. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 3.
- 20 44. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 4.
45. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 5.
46. A plurality of isolated nucleic acid molecules that correspond to two or more of the  
25 markers of claim 6.

47. The method of claim 31, wherein said ESTs comprise a length of greater than 100 nucleotides.

48. An array consisting essentially of the plurality of nucleic acid molecules of claim 41.

49. An array consisting essentially of the plurality of nucleic acid molecules of claim 42.

5 50. An array consisting essentially of the plurality of nucleic acid molecules of claim 43.

51. An array consisting essentially of the plurality of nucleic acid molecules of claim 44.

52. An array consisting essentially of the plurality of nucleic acid molecules of claim 45.

53. An array consisting essentially of the plurality of nucleic acid molecules of claim 46.

54. A kit for diagnosing or prognosing schizophrenia, comprising:

10 a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3, claim 4, claim 5 and claim 6; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means  
15 capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means; wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

20 55. A kit for diagnosing or prognosing schizophrenia as compared with manic depression syndrome, comprising:

a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3, claim 4, claim 5 and claim 6; wherein said first  
25 priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

- b) an enzyme with reverse transcriptase activity,
- c) an enzyme with thermostable DNA polymerase activity, and
- d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene  
 5 in a test subject.

56. A kit for monitoring a course of therapeutic treatment of schizophrenia, comprising:

a) two gene-specific priming means designed to produce double stranded DNA  
 complementary to a gene that corresponds to a marker selected from the group consisting of  
 the markers of claim 1, claim 2, claim 3, claim 4, claim 5 and claim 6; wherein said first  
 10 priming means contains a sequence which can hybridize to RNA, cDNA or an EST  
 complementary to said gene to create an extension product and said second priming means  
 capable of hybridizing to said extension product;

- b) an enzyme with reverse transcriptase activity,
- c) an enzyme with thermostable DNA polymerase activity, and
- 15 d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene  
 in a test subject.

57. A kit for monitoring progression or regression of schizophrenia, comprising:

a) two gene-specific priming means designed to produce double stranded DNA  
 20 complementary to a gene that corresponds to a marker selected from the group consisting of  
 the markers of claim 1, claim 2, claim 3, claim 4, claim 5 and claim 6; wherein said first  
 priming means contains a sequence which can hybridize to RNA, cDNA or an EST  
 complementary to said gene to create an extension product and said second priming means  
 capable of hybridizing to said extension product;

- 25 b) an enzyme with reverse transcriptase activity,
- c) an enzyme with thermostable DNA polymerase activity, and
- d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene  
 in a test subject.

58. The kits of any one of claims 54 - 57 wherein said gene-specific priming means correspond to a gene selected from the group consisting of the genes listed in Table 3Y and Table 3AC

59. A plurality of nucleic acid molecules that identify or correspond to two or more genes  
5 selected from the group consisting of the genes listed in Table 3Y and Table 3AC.

60. The method of claim 32, wherein said ESTs comprise a length of greater than 100 nucleotides.